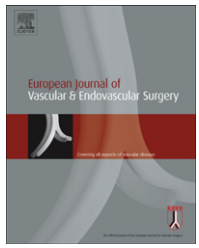
Eur J Vasc Endovasc Surg (2009) **38**, 623–626



COCHRANE REVIEWS

Cochrane Peripheral Vascular Diseases Review Group: Review Abstracts

Introduction

The following abstracts are part of an ongoing series of articles produced by the Cochrane Peripheral Vascular Diseases Review Group, which is part of The Cochrane Collaboration. The reviews are published in full in *The Cochrane Database of Systematic Reviews* in *The Cochrane Library*, a quarterly electronic journal available on CD-ROM and via the Internet (http://www3.interscience.wiley.com/cgi-bin/mrwhome/106568753/HOME). The electronic format allows Cochrane reviews to accommodate new data as they become available, making *The Cochrane Library* a consistently up-to-date source of information over time.

Certain abstracts appearing in *The Cochrane Database of Systematic Reviews* may be presented in a simpler, less scientific format than the abstract presented here to permit greater accessibility to the public. However, the substance of both versions is the same. Cochrane reviews are now indexed on MEDLINE.

If you are interested in conducting a Cochrane review or contributing to the activities of the Cochrane Peripheral Vascular Diseases Review Group, please contact:

Professor FGR Fowkes
Cochrane Peripheral Vascular Diseases Review Group
Public Health Sciences
University of Edinburgh
Teviot Place
Edinburgh EH8 9AG
Tel. +44 (0) 131 650 3220
Fax. +44 (0) 131 650 6904

Any feedback on Cochrane reviews should be made through the feedback facility on *The Cochrane Library*, or by contacting the group at the above address.

Abstracts

Abstract. Naftidrofuryl for intermittent claudication

de Backer TLM, Vander Stichele R, Lehert P, Van Bortel L. Naftidrofuryl for intermittent claudication. Cochrane Database of Systematic Reviews 2008 , Issue 2 . Art. No.: CD001368. DOI: 10.1002/14651858.CD001368.pub3 .

Background

Lifestyle changes and cardiovascular prevention measures are a primary treatment for intermittent claudication (IC). Symptomatic treatment with vasoactive agents (Anatomic Therapeutic Chemical Classification (ATC) for medicines from the World Health Organisation class CO4A) is controversial.

Objectives

To evaluate evidence on the efficacy and safety of oral naftidrofuryl (ATC CO4 21) versus placebo on the pain-free walking distance (PFWD) of people with IC by using a meta-analysis based on individual patient data (IPD).

Search strategy

The Cochrane Peripheral Vascular Diseases Group searched their Trials Register (last searched December 2007) and CENTRAL (last searched 2007, Issue 4). We searched MEDLINE, EMBASE, International Pharmaceutical Abstracts, the Science Citation Index and contacted the authors and checked the reference lists of retrieved articles. We asked the manufacturing company for IPD.

Selection criteria

We included only randomized controlled trials (RCTs) with low or moderate risk of bias for which the IPD were available.

Data collection and analysis

We collected data from the electronic data file or from the case report form and checked the data by a statistical quality control procedure. All randomized patients were analyzed

1078-5884/$36
doi:10.1016/j.ejvs.2009.06.019

following the intention-to-treat (ITT) principle. The geometric mean of the relative improvement in PFWD was calculated for both treatment groups in all identified studies.

The effect of the drug was assessed compared with placebo on final walking distance (WDf) using multilevel and random-effect models and adjusting for baseline walking distance (WD0). For the responder analysis, therapeutic success was defined as an improvement of walking distance of at least 50%.

Main results

We included seven studies in the IPD (n = 1266 patients). One of these studies (n = 183) was only used in the sensitivity analysis so that the main analysis included 1083 patients. The ratio of the relative improvement in PFWD (naftidrofuryl compared with placebo) was 1.37 (95% confidence interval (CI) 1.32 to 1.51, $P < 0.001$). The absolute difference in responder rate, or proportion successfully treated, was 22.3% (95% CI 17.1% to 27.6%). The calculated number needed to treat was 4.5 (95% CI 3.6 to 5.8).

Authors' conclusions

Naftidrofuryl has a statistically significant and clinically meaningful effect of improving walking distance in the six months after initiation of therapy for people with intermittent claudication. Access by researchers to data from RCTs that are suitable for IPD analysis should be possible through repositories of data from pharmacological trials. Regular formal appraisal of the balance of risk and benefit is needed for older pharmaceutical products.

Abstract. Beta blockers for peripheral arterial disease

Paravastu SC, Mendonca D, Da Silva A. Beta blockers for peripheral arterial disease. Cochrane Database of Systematic Reviews 2005 , Issue 4 . Art. No.: CD005508. DOI: 10.1002/14651858.CD005508 .

Background

Beta (ß) blockers are indicated for use in coronary artery disease (CAD). However, optimal therapy for people with CAD accompanied by intermittent claudication has been controversial due to the presumed peripheral haemodynamic consequences of beta blockers, leading to worsening symptoms of intermittent claudication.

Objectives

To quantify the potential harm of beta blockers on maximum walking distance, claudication distance, calf blood flow, calf vascular resistance, and skin temperature when used in patients with peripheral arterial disease (PAD).

Search strategy

The Cochrane Peripheral Vascular Diseases (PVD) Group searched for publications describing randomised controlled trials (RCTs) of beta blockers in PAD in their Trials Register (last searched 6 May 2008) and the Cochrane Central Register of Controlled Trials (CENTRAL) (last searched *The Cochrane Library* 2008, Issue 2). We handsearched relevant journals and conference proceedings.

Selection criteria

Randomised controlled trials evaluating the role of both selective (ß1) and non-selective (ß1 and ß2) beta blockers compared with placebo. We excluded trials comparing different types of beta blockers.

Data collection and analysis

Primary outcome measures were claudication distance in metres, and the time to claudication in minutes, and maximum walking distance in metres and minutes (as assessed by treadmill).

Secondary outcome measures were calf blood flow (ml/100 ml/min), calf vascular resistance, and skin temperature (°C).

Main results

We included six RCTs fulfilling the above criteria, with a total of 119 patients. The beta blockers studied were atenolol, propranolol, pindolol, and metoprolol. None of the trials showed a statistically significant worsening effect of beta blockers on either the primary or secondary outcomes. There were no reports of any adverse events with the beta blockers studied.

Authors' conclusions

There is currently no evidence that beta blockers adversely affect walking distance in people with intermittent claudication. However, due to the lack of large published trials beta blockers should be used with caution if clinically indicated.

Abstract. Combined intermittent pneumatic leg compression and pharmacological prophylaxis for prevention of deep venous thrombosis in high-risk patients

Kakkos SK, Caprini JA, Geroulakos G, Nicolaides AN, Stansby GP, Reddy DJ. Cochrane Database of Systematic Reviews 2005 , Issue 2. Art. No.: CD005258. DOI: 10.1002/14651858.CD005258.

Background

It has been suggested that combined modalities (methods of treatment) are more effective than single modalities in preventing venous thromboembolism (defined as deep vein thrombosis and pulmonary embolism, or both) in high-risk patients.

Objectives

To assess the efficacy of intermittent pneumatic leg compression combined with pharmacological prophylaxis

versus single modalities in preventing venous thromboembolism in high-risk patients.

Search strategy

The Cochrane Peripheral Vascular Diseases (PVD) Group searched their Specialized Register (last searched 17 July 2007) and the Cochrane Central Register of Controlled Trials (CENTRAL) (last searched *The Cochrane Library* 2008, Issue 3). We searched the reference lists of relevant articles to identify additional trials.

Selection criteria

Randomized controlled trials (RCTs) or controlled clinical trials (CCTs) of combined intermittent pneumatic leg compression and pharmacological interventions used to prevent venous thromboembolism in high-risk patients.

Data collection and analysis

Data extraction was undertaken independently by two review authors using data extraction sheets provided by the Cochrane PVD Group.

Main results

Eleven studies, six of them randomized controlled trials, were identified. The trials included 7431 patients, in total. Compared with compression alone, the use of combined modalities reduced significantly the incidence of both symptomatic pulmonary embolism (PE) (from about 3% to 1%; odds ratio (OR) 0.39, 95% confidence interval (CI) 0.25 to 0.63) and deep vein thrombosis (DVT) (from about 4% to 1%; OR 0.43, 95% CI 0.24 to 0.76). Compared with pharmacological prophylaxis alone, the use of combined modalities significantly reduced the incidence of DVT (from 4.21% to 0.65%; OR 0.16, 95% CI 0.07 to 0.34) but the included studies were underpowered with regard to PE. The comparison of compression plus pharmacological prophylaxis versus compression plus aspirin showed a non-significant reduction in PE and DVT in favor of the former group. Repeat analysis restricted to the RCTs confirmed the above findings.

Authors' conclusions

Compared with compression alone, combined prophylactic modalities decrease significantly the incidence of venous thromboembolism. Compared with pharmacological prophylaxis alone, combined modalities reduce significantly the incidence of DVT but the effect on PE is unknown. The results of the current review support, especially in high-risk patients, the use of combined modalities. More studies on their role in the prevention of PE, compared with pharmacological prophylaxis alone, are urgently needed.

Abstract. Low molecular weight heparin for prevention of venous thromboembolism in patients with lower-leg immobilization

Testroote M, Stigter WAH, de Visser DC, Janzing HMJ. Low molecular weight heparin for prevention of venous thromboembolism in patients with lower-leg immobilization. Cochrane Database of Systematic Reviews 2008 , Issue 4 . Art. No.: CD006681. DOI: 10.1002/14651858.CD006681.pub2.

Background

Immobilization of the lower leg is associated with venous thromboembolism. Low molecular weight heparin (LMWH) is an anticoagulant treatment which might be used in adult patients with lower-leg immobilization to prevent deep venous thrombosis and its complications.

Objectives

To investigate the current literature on thromboprophylactic practice for patients with lower-limb injuries who are immobilized in plaster casts or braces, to assess the need for concrete guidelines, and to assess whether it is possible to come to an evidence-based conclusion.

Search strategy

The Cochrane Peripheral Vascular Disease Group searched their Trials Register (last searched 20 May 2008) and the Central Register of Controlled Trials (CENTRAL) (last searched *The Cochrane Library* 2008, Issue 2). We searched MEDLINE (until May 2008) and EMBASE (until May 2008) and reference lists of articles. We contacted pharmaceutical companies of LMWHs for relevant studies.

Selection criteria

Randomized controlled trials (RCTs) and controlled clinical trials (CCTs) that described thromboprophylaxis by means of LMWH compared with no prophylaxis or placebo in adult patients with lower-leg immobilization. Immobilization was by means of a plaster cast or brace.

Data collection and analysis

Two authors independently assessed trial quality and extracted data. The review authors contacted the trial authors for additional information. Statistical analysis was carried out using Review Manager (RevMan 5).

Main results

We included six RCTs fulfilling the above criteria with a total of 1490 patients. We found an incidence of venous thromboembolism ranging from 4.3% to 40%, in patients who had a leg injury that had been immobilized in a plaster cast or a brace for at least one week and who received no prophylaxis, or placebo. This number was significantly lower in patients who received daily subcutaneous injections of LMWH during immobilization (event rates ranging

from 0% to 37%; odds ratio (OR) 0.49; fixed 95% confidence interval (CI) 0.34 to 0.72; with minimal evidence of heterogeneity with an I^2 of 20%, P = 0. 29). Comparable results were seen in the following subcategories: patients who had undergone operations, conservatively treated patients, patients with fractures, patients with soft-tissue injuries, patients with proximal thrombosis, patients with distal thrombosis and patients with below-knee casts. Complications of major bleeding events were extremely rare (0.3%) and there were no reports of heparin-induced thrombocytopenia.

Authors' conclusions

Use of LMWH in outpatients significantly reduces VTE when immobilization of the lower leg is required.